FORM PTO-1390 (REV 10-94) U.S. DEPARTMENT OF COMMERCE PATENT AND TRADEMARK OFFICE

TRANSMITTAL LETTER TO THE UNITED STATES DESIGNATED/ELECTED OFFICE (DO/EO/US) CONCERNING A FILING UNDER 35 U.S.C. 371

ATTORNEY'S DOCKET NUMBER: 10642.9USWO

U.S. APPLICATION NO. (If known, see 37 C.F.R. 1.5): unknown 10/018027

INTERNATIONAL APPLICATION NO.	INTERNATIONAL FILING DATE	PRIORITY DATE CLAIMED
PCT/IB00/00730	31 May 2000	10 June 1999

TITLE OF INVENTION

MEDICAL MEMBRANE FOR STIMULATING TISSUE FORMATION

APPLICANT(S) FOR DO/EO/US

HORVATH et al.

Applicant herewith submits to the United States Designated/Elected Office (DO/EO/US) the following items and other information:

1. [X] This is a **FIRST** submission of items concerning a filing under 35 U.S.C. 371.
2. [ ] This is a **SECOND** or **SUBSEQUENT** submission of items concerning a filing under 35 U.S.C. 371.
3. [X] This express request to begin national examination procedures (35 U.S.C. 371(f)) at any time rather than delay examination until the expiration of the applicable time limit set in 35 U.S.C. 371(b) and PCT Articles 22 and 39(l).
4. [x] A proper Demand for International Preliminary Examination was made by the 19th month from the earliest claimed priority date.

5. [X] A copy of the International Application as filed (35 U.S.C. 371(c)(2))
   a. [x] is transmitted herewith (required only if not transmitted by the International Bureau).
   b. [X] has been transmitted by the International Bureau.
   c. [ ] is not required, as the application was filed in the United States Receiving Office (RO/US).
6. [x] A translation of the International Application into English (35 U.S.C. 371(c)(2)).

7. [X] Amendments to the claims of the International Application under PCT Article 19 (35 U.S.C. 371(c)(3))
   a. [ ] are transmitted herewith (required only if not transmitted by the International Bureau).
   b. [ ] have been transmitted by the International Bureau.
   c. [ ] have not been made; however, the time limit for making such amendments has NOT expired.
   d. [x] have not been made and will not be made.

8. [ ] A translation of the amendments to the claims under PCT Article 19 (35 U.S.C. 371(c)(3)).

9. [X] An unsigned oath or declaration of the inventor(s) (35 U.S.C. 371 (c)(4)).

10. [x] A translation of the annexes to the International Preliminary Examination Report under PCT Article 36 (35 U.S.C. 371(c)(5)).

Items 11. to 16. below concern document(s) or information included:

11. [ ] An Information Disclosure Statement under 37 CFR 1.97 and 1.98.

12. [ ] An assignment document for recording. A separate cover sheet in compliance with 37 CFR 3.28 and 3.31 is included.

13. [X] A FIRST preliminary amendment.
    [ ] A SECOND of SUBSEQUENT preliminary amendment.

14. [ ] A substitute specification.

15. [ ] A change of power of attorney and/or address letter.

16. [x] Other items or information: International Publication Page, Preliminary Amendment, Marked-up Copy, Abstract, Form Pct/ISA/210, Form PCT/IB/304, Form PCT/IPEA/409 with annexes, 4 Sheets of Drawings

U.S. APPLICATION NO. (If known, see 37 C.F.R. 1.5)	INTERNATIONAL APPLICATION NO.	ATTORNEY'S DOCKET NUMBER
unknown 10/018027	PCT/IB00/00730	10642.9USWO

17. [X] The following fees are submitted:	CALCULATIONS PTO USE ONLY	
BASIC NATIONAL FEE (37 CFR 1.492(a) (1)-(5)):		
Search Report has been prepared by the EPO or JPO **$890.00**		
International preliminary examination fee paid to USPTO (37 CFR 1.492(a)(1)) **$710.00**		
No international preliminary examination fee paid to USPTO (37 CFR 1.482) but international search fee paid to USPTO (37 CFR 1.445(a)(2)) **$740.00**		
Neither international preliminary examination fee (37 CFR 1.482) nor international search fee (37 CFR 1.445(a)(3)) paid to USPTO **$1040.00**		
International preliminary examination fee paid to USPTO (37 CFR 1.482) and all claims satisfied provisions of PCT Article 33(2)-(4) **$100.00**		
ENTER APPROPRIATE BASIC FEE AMOUNT =	**$890.00**	
Surcharge of **$130.00** for furnishing the oath or declaration later than [ ] 20 [ ] 30 months from the earliest claimed priority date (37 CFR 1.492(e)).	$	

CLAIMS	NUMBER FILED		NUMBER EXTRA	RATE		
Total claims	30	-20 =	9	X **$18.00**	**$162.00**	
Independent claims	4	-3 =	1	X **$84.00**	**$84.00**	
MULTIPLE DEPENDENT CLAIM(S) (if applicable)				+ **$260.00**	$	
TOTAL OF ABOVE CALCULATIONS =					**$1136.00**	
Reduction by 1/2 for filing by small entity, if applicable. Small entity status is claimed pursuant to 37 CFR 1.27					**$1136.00**	
SUBTOTAL =					**$1136.00**	
Processing fee of **$130.00** for furnishing the English translation later than [ ] 20 [ ] 30 months from the earliest claimed priority date (37 CFR 1.492(f). +					$	
TOTAL NATIONAL FEE =					**$1136.00**	
Fee for recording the enclosed assignment (37 CFR 1.21(h)). The assignment must be accompanied by an appropriate cover sheet (37 CFR 3.28, 3.31). $40.00 per property +					$	
TOTAL FEES ENCLOSED =					**$1136.00**	
					Amount to be: refunded	$
					charged	$

a. [X] Check(s) in the amount of $1136.00 to cover the above fees is enclosed.

b. [ ] Please charge my Deposit Account No. _____ in the amount of $ _____ to cover the above fees. A duplicate copy of this sheet is enclosed.

c. [X] The Commissioner is hereby authorized to charge any additional fees which may be required, or credit any overpayment to Deposit Account No. 13-2725.

NOTE: Where an appropriate time limit under 37 CFR 1.494 or 1.495 has not been met, a petition to revive (37 CFR 1.137(a) or (b)) must be filed and granted to restore the application to pending status.

SEND ALL CORRESPONDENCE TO:
John J. Gresens
MERCHANT & GOULD
P.O. Box 2903
Minneapolis, MN 55402-0903

SIGNATURE: John J. Gresens

NAME: John J. Gresens

REGISTRATION NUMBER: 33,112

10/018027

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

JC10 Rec'd PCT/PTO 10 DEC 2001

Applicant: HORVATH et al.

Docket: 10642.9USWO

Title: MEDICAL MEMBRANE FOR STIMULATING TISSUE FORMATION

CERTIFICATE UNDER 37 CFR 1.10
'Express Mail' mailing label number: EV037644216US
Date of Deposit: 10 December 2001
I hereby certify that this paper or fee is being deposited with the United States Postal Service 'Express Mail Post Office To Addressee' service under 37 CFR 1.10 and is addressed to the Commissioner for Patents, Washington, D.C. 20231.

By: _____
Name: Chris Stordahl

BOX PCT
Commissioner for Patents
Washington, D.C. 20231

Sir:

We are transmitting herewith the attached:

- ☒ Transmittal sheet, in duplicate, containing Certificate under 37 CFR 1.10.
- ☒ National Stage PCT Patent Application: Spec. 14 pgs; 29 claims; Abstract 1 pgs. The fee has been calculated as shown below in the 'Claims as Filed' table.
- ☒ 4 sheets of formal drawings
- ☒ An unsigned Combined Declaration and Power of Attorney
- ☒ A check in the amount of $974.00 to cover the Filing Fee
- ☒ Other: International Publication Page, Courtesy Copy of PCT/IB00/00730 in German, Preliminary Amendment, Marked-up Copy, Abstract, Form PCT/ISA/210, Form PCT/IB/304, Form PCT/IPEA/409 with annexes, English translation of annex to International Preliminary Examination Report, Form PTO-1390
- ☒ Return postcard

CLAIMS AS FILED

Number of Claims Filed		In Excess of:		Number Extra		Rate		Fee
Basic Filing Fee								$890.00
Total Claims								
14	-	20	=	0	x	18.00	=	$0.00
Independent Claims								
4	-	3	=	1	x	84.00	=	$84.00
MULTIPLE DEPENDENT CLAIM FEE								$0.00
TOTAL FILING FEE								$974.00

Please charge any additional fees or credit overpayment to Deposit Account No. 13-2725. A duplicate of this sheet is enclosed.

MERCHANT & GOULD P.C.
P.O. Box 2903, Minneapolis, MN 55402-0903
(612) 332-5300

By: _____
Name: John J. Gresens
Reg. No.: 33,112
Initials: JJG:hjh

23552
PATENT TRADEMARK OFFICE

S/N unknown PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant:	HORVATH et al.	Serial No.:	unknown
Filed:	concurrent herewith	Docket No.:	10642.9USWO
Title:	MEDICAL MEMBRANE FOR STIMULATING TISSUE FORMATION		

CERTIFICATE UNDER 37 CFR 1.10
'Express Mail' mailing label number: EV037644216US
Date of Deposit: 10 December 2001
I hereby certify that this correspondence is being deposited with the United States Postal Service 'Express Mail Post Office To Addressee' service under 37 CFR 1.10 on the date indicated above and is addressed to the Assistant Commissioner for Patents, Washington, D.C . 20231.

By: _____
Name: Chris Stordahl

PRELIMINARY AMENDMENT

Box PCT
Assistant Commissioner for Patents
Washington, D.C. 20231

Dear Sir:

In connection with the above-identified application filed herewith, please enter the following preliminary amendment, based on claims amended in prosecution of the international application under Article 36, and published in the International Preliminary Examination Report, a copy of which is enclosed.

IN THE ABSTRACT

Insert the attached Abstract page into the application as the last page thereof.

IN THE SPECIFICATION

A courtesy copy of the present specification is enclosed herewith. However, the World Intellectual Property Office (WIPO) copy should be relied upon if it is already in the U.S. Patent Office.

IN THE CLAIMS

Please amend claim 28 as follows:

28. (Amended) Kit for the treatment of pulp exposures comprising at least a medical membrane (1-6) which comprises at least one roughened surface which has a porous and/or reticular structure, and a device for the application of a medical membrane in a cavity of claim 26.

REMARKS

The above preliminary amendment is made to remove multiple dependencies from claims 28.

A new abstract page is supplied to conform to that appearing on the publication page of the WIPO application, but the new Abstract is typed on a separate page as required by U.S. practice.

Attached hereto is a marked-up version of the changes made to the claims by the current amendment. The attached page is captioned "Marked-up Copy".

Applicants respectfully request that the preliminary amendment described herein be entered into the record prior to calculation of the filing fee and prior to examination and consideration of the above-identified application.

If a telephone conference would be helpful in resolving any issues concerning this communication, please contact Applicants' primary attorney-of record, John J. Gresens (Reg. No. 33,112), at (612) 371.5265.

Respectfully submitted,

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Dated: 10 December 2001

By _____
John J. Gresens
Reg. No. 33,112

JJG:hjh

10642.9USWO

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28. Kit for the treatment of pulp exposures comprising at least a medical membrane (1-6) which comprises at least one roughened surface which has a porous and/or reticular structure, and a device for the application of a medical membrane in a cavity of claim[s] 26 [and 27].

Medical membrane for stimulating tissue formation

Cross References to Related Applications

This application claims the priority of German patent application No. 199 26 438.4, filed June 10, 1999 and of German patent application No. 199 48 787.1, filed October 10, 1999 the disclosure of which is incorporated herein by reference in its entirety.

Technical Field

The present application relates to a medical membrane as well as to a method for the application of a medical membrane in dentistry.

Background Art

In the context of healing processes medical membranes allow a selective influence on cell types with different growth rates and attachment characteristics, respectively, which are available in the wound area. Undesired cell types with higher growth rates are e.g. hindered to invade the wound area and the attachment of cells which form the new tissue is stimulated. This method is referred to as "guided tissue regeneration". The term "guided bone regeneration" is used if the application of medical membranes selectively hinders fast growing epithelium cells and connective tissue cells to invade the wound area and to proliferate therein and thereby enables slow growing bone cells to heal the tissue defect.

Medical membranes are made of various materials. Reabsorbable membranes are made of collagen or polylactic/polyglycolide acid polymer or copolymer, re-

spectively. Non-reabsorbable membranes are made of polytetrafluorethylene. Reabsorbable membranes remain in situ; non-reabsorbable membranes are removed after completion of their task.

Studies have shown that medical membranes which were developed in wound repair studies e.g. collagen or polytetrafluorethylene can stimulate the attachment and integration of fibroblasts or other cells forming new tissue as well as wound closure.

Furthermore, in vitro as well as in vivo studies have shown the importance of mechanical stability, sterility and absence of inflammation for the preservation of the pulp after its exposure by a trauma or in the context of restorative measures or partial resection, respectively. In order to preserve the vitality of the pulp it is as well important to avoid the formation of a cavity below the filling due to shrinkage of the blood clot and to avoid a wound treatment harming the pulp and it is important to achieve a bacteria impermeable sealing of the dentine wound. Nowadays most often applied method is to produce a scurf of the pulp and said method is very harmful to the pulp and to its ability to regenerate and therefore new means are needed which allow a less harmful pulp treatment.

The present invention has the aim to provide means in order to improve the preservation of the pulp vitality.

Disclosure of the Invention

Said aim is accomplished by a medical membrane according to claim 1.

Hence, it is a general object of the invention to provide a medical membrane for the arrangement in a cavity of the dentine of a tooth for the capping of a pulpal wound. It is shown that due to the protection of the membrane the ability of the pulp to regenerate and

its vitality is improved. Besides direct pulp exposures, deep dentine wounds are generated by injuring dentine channels which leads to a serious burden for the pulp and the pulp is injured in this way.

A membrane which is essentially impermeable to a sealant or for a cement is preferred. The term "essentially impermeable" means that the membrane is impermeable to substances which can disturb the pulp regeneration and/or dentine regeneration.

Preferred is a membrane which comprises at least one roughened surface allowing the attachment of fibrin fibers, the attachment and ingrowth of pulpal fibroblasts and of other cells.

In a preferred embodiment the roughened surface has a porous and/or reticular structure. However, said porous and/or reticular structure of the membrane allows diffusion of molecules and ions through the membrane. On the one hand the membrane comprises a roughened surface which has preferably a porous and/or reticular structure, on the other hand said membrane is at least impermeable to substances disturbing the pulp regeneration to protect the pulp. This can e.g. be achieved by a bilayer design. Said bilayer design is characterized by a denser structure of the membrane side facing away from the pulp and thereby impermeability of the membrane is obtained. In a further embodiment, diffusion of harmful substances is prevented by an uniformly structured membrane wherein the side of said membrane facing away from the pulp comprises a differently structured, in particular an impermeable layer or coating. However, said membrane has to be so impermeable to prevent at least temporarily diffusion of substances disturbing pulp regeneration or dentine regeneration so that an impermeable sealing, preferably a hardening coating, after application of the membrane is possible.

In order to facilitate anchorage of fibrin fibers and ingrowth of fibroblasts or other regenerative

cells it is proposed that the percentage of the pores or of the mesh of the porous or reticular surface which is in contact with the pulp is higher than 20%, preferably higher than 50%. The percentage of pores or the mesh, respectively, promotes attachment and integration of regenerative cells and thereby provides wound healing and the vitality of the pulp is preserved, preferably followed by a curing material which closes the pulp exposure.

A particular good integration of regenerative cells is seen if the average diameter of the pores or the width of the mesh lies between 0.5 µm and 200 µm, preferably between 1 µm and 100 µm.

Preferred is a membrane which is self adhesive to the dental hard tissues or which due to an adhesive coating is adhesive to the dental hard tissues without harming the pulp so that the sealant which preferably shows adhesion to the dental hard tissues such as e.g. glassionomer cement or light hardening glassionomer cement, is neither in direct nor indirect contact with the pulp due to the impermeability of the membrane.

The medical membrane according to the present invention forms per se or preferably after sealing with a hardening material or after coating, respectively, a preferably hard and impermeable barrier on the one hand between the pulp exposure and adjacent dental hard tissues and on the other hand between the restorative material above the sealed or coated membrane wherein said restorative material partially or fully replaces the missing dental hard tissues. The impermeability of the membrane which said membrane shows per se or which is achieved by overlaying the membrane with a restorative material provides for that substances neither can diffuse from the pulp to the restorative material nor from the restorative material to the pulp. Therefore, the membrane is either per se or after overlaying with restorative material impermeable to the penetration of liquids such as blood, serum and water. In addition, the membrane is bio-

logically impermeable to cells and microorganisms and where required for the biocompatibility the membrane is chemically impermeable to molecules and ions disturbing the pulp regeneration and dentine regeneration.

Preferred is a membrane which has a surface of less than 100mm^2, preferably less than 50 mm^2. The nowadays available size units of medical membranes are not only due to lack of adhesion, thickness and impermeability unsuitable for the capping of a pulp wound. In practice, this kind of membranes can as well not be cut to the appropriate size since the membranes have to be very small and sterile and thus the cutting of an opened membrane to the appropriate size and its adaptation increases the risk for infections which is not acceptable. The remaining pieces of the expensive membranes can not be stored for sterility reasons.

Only the construction of known medical membranes or dental membranes, respectively, as membrane pads in an applicable form enables their use in pulp regeneration and dentine regeneration. Said membranes open via guided cell proliferation and formation of new tissues a new field which as "guided pulp regeneration" or "guided dentine regeneration", respectively, adds a new field to the known fields of guided tissues regeneration and guided bone regeneration. The preparation of membrane pads having a size of less than 100 mm^2, preferably less than 50 mm^2, from known medical membranes, the modification of the membrane structure and the improved impermeability of the membrane surface facing away from the pulp constitute an essential inventive step which enables the use of membranes with limited permeability in the field of pulp regeneration and dentine regeneration.

Positive practical results were achieved with membrane pads having a thickness of less than 3 mm, preferably less than 0.5 mm. Since thin membranes can have a porosity or density, respectively, which is sufficient

for dentine regeneration, the use of thin membranes is preferred due to the improved capability of adaptation.

Since the membrane pads are preferably used inside of usually concave cavities or of fracture faces, it is proposed that said membrane pads preferably have an oval or round shape. Such a shaped membrane pad can be optimally arranged in a hemispherical cavity which is the result of dentine caries excavation. A 1 to 2 mm wide seating which is preferably self adhesive on the dentine surrounding the pulpal wound, enables a reliable and provisional impermeable positioning of the membrane.

Preferred is a membrane with a concave or convex shape. The concave, convex or straight variants of the membrane enable depending on the individual case a cupola-like cover of the exposed pulp or a close fit of the membrane to the concavity of the cavity.

In a preferred embodiment the membrane comprises a cover foil which is biologically and chemically impermeable and which preferably fully covers or optionally fully overlaps all sides of the membrane wherein the pad free marginal part of the cover foil which is on the side of the pulp preferably is self adhesive like an adhesive dressing. Said cover foil facilitates the precise positioning of the membrane pad inside a cavity of a tooth. Furthermore, said cover foil allows an impermeable, adhesive connection to the dentine and acts as a barrier towards the suprastructure.

Good results can be achieved with membranes which are made of a non-reabsorbable material such as e.g. polytetrafluoroethylene or preferably titanium. Said membranes are not rejected by the body and titanium is suitable on the one hand for the production of porous structures and on the other hand very good as impermeable material.

Good results can as well be achieved with membranes which are made of reabsorbable material, preferably collagen. Said membranes especially promote at-

tachment and integration of pulp fibroblasts and other regenerative cells and are temporarily sufficiently impermeable to a sealing, hardening material or can be made biologically and chemically impermeable by means of a cover foil.

The membranes are preferably resistant to tearing but can be cut. A soft, sheet-like construction of the membranes makes them arbitrarily deformable and adaptive. Reinforcements of the membrane body or structural modifications can e.g. be achieved by means of titanium lamination or other biologically inert materials. An individual three dimensional shape can be achieved by membranes which e.g. due to reinforcements are plastically deformable ("bleitot").

The surface of the membrane facing away from the pulp and therefore in contact with the restorative material is preferably inert so that there is no interconnection with the restorative material in order to completely avoid that shrinking forces caused by the polymerization of the restorative material are transferred to the membrane. Said inertia is preferably achieved by teflonisation, hydrophilicity or the use of a non-radically polymer.

In a further embodiment the surface of the membrane facing away from the pulp and thus in contact with the restorative material forms a mechanical or adhesive bonding to the restorative material in order to assure a impermeable seal of the membrane based pulp capping. Said bonding is preferably achieved by interlocking, entanglement, homo polymerization or co-polymerization or secondary or primary chemical bonds. A tight, mechanical and/or adhesive connection to the dental hard tissues, in particular to the dentine, is preferably achieved by means of dentine adhesion, preferably after activation of the adjacent dentine. This can also be achieved by interlocking, entanglement, homo polymeri-

zation or co-polymerization as well as secondary or primary chemical bonds.

The inner surface which is in contact with the pulp and thus facing away from the restoration material is preferably biocompatible, promoting attachment or cell integration, respectively, and sterile.

Furthermore, growth factors or bone morphogenic proteins can be added to the membrane or pharmacological effects can be achieved by the membrane such as e.g. soft or hard chemotherapeutical effects which are based on bakteriostatic or bactericidal effects. Finally, tissue stimulating effects leading to e.g. forming of tertiary dentine can be supported by a particular construction of the membrane.

Brief Description of the Drawings

Embodiments of medical membranes according to the invention and their use for the regeneration of the pulp or the regeneration of the dentine are shown in the drawings and are further explained below.

It shows:

Figure 1a a small round membrane with round overlapping carrier foil,

Figure 1b a small round membrane with round carrier foil which has the size of the membrane,

Figure 1c a small round membrane without carrier foil,

Figure 2a a bigger round membrane with a round overlapping carrier foil,

Figure 2b a bigger round membrane with a round carrier foil which has the size of the membrane,

Figure 2c a bigger round membrane without a carrier foil,

Figure 3a a big round membrane with a round overlapping carrier foil,

Figure 3b a big round membrane with a round carrier foil which has the size of the membrane,

Figure 4a a small quadratic membrane with a quadratic overlapping carrier foil,

Figure 4b a small quadratic membrane with a quadratic carrier foil with the size of the membrane,

Figure 4c a small quadratic membrane without a carrier foil,

Figure 5a an oval membrane with an oval overlapping carrier foil,

Figure 5b an oval membrane with an oval carrier foil which has the size of the membrane,

Figure 5c an oval membrane without a carrier foil,

Figure 6a a rectangular membrane with a rectangular carrier foil which has the size of the membrane,

Figure 6b a rectangular membrane with a rectangular carrier foil overlapping the membrane,

Figure 6c a rectangular membrane without a carrier foil,

Figure 7 a section through a tooth with a cavity on the right side,

Figure 8 a section through a tooth with a big and deep two-faced cavity,

Figure 9 a section through a tooth with a deeper cavity on the right side,

Figure 10 a three dimensional drawing of a tooth with a cavity and positioned membrane,

Figure 11 a section through a tooth with positioned membrane and restorative material,

Figure 12 a magnified part of figure 11 and

Figure 13 a device for the application of a medical membrane.

Figures 1 to 6 show different embodiments of membranes 1 to 6. Each of said membrane consists of a porous membrane part 7 to 12 and a dense carrier foil 13 to 18. The carrier foil 13 to 18 is bigger than the membrane part 7 to 12 so that said carrier foil is overlapping the membrane 7 to 12. The carrier foil 13 to 18 can as well have the same size as the membrane 7 to 12 (13' to 18'). Instead of the carrier foil 13 to 18 or 13' to 18', respectively, a coating of the membrane in situ can be used wherein said coating is performed after the primarily adhesive membrane without a carrier foil 7' to 12' has been positioned on the adjacent dentine.

The medical membranes shown in figures 1 to 6 are just embodiments for often used shapes. Depending on the use it is as well possible to apply or use other shapes of medical membranes with or without carrier foils and with or without a suprastructure, respectively.

Said medical membranes 1 to 6 have the function to cover in cavities the area where the pulp is exposed. Examples for such cavities are shown in figures 7 to 9. In figure 7 a cavity 19 of a tooth 20 is shown wherein said cavity cuts in the area 21 the pulp 22. Thereby a sectional plane 23 is formed. In the present case, said sectional plane cuts a circular area of at least 1 to 2 mm width out of the dentine adjacent to the pulp 22 wherein said circular area lies in the plane of sectional plane 23. Said area adjacent to the open pulp serves as contact surface for a membrane 1 to 6.

Figure 8 shows another cavity 24 of a tooth 25 in which the left branch of the pulp 26 is cut. Said cavity 24 has as well around the sectional area 27 of the pulp 26 an at least circular contact surface 28 of dentine.

Figure 9 shows a pulp 30 of a tooth 31 wherein said pulp is cut by a cavity 29. Thereby the sectional plane 32 lies between cavity 29 and pulp 30 in a

perpendicular plane wherein around the section area 33 an at least circular contact surface 34 of dentine exists.

The formed contact surface around the cut pulp can as well lie transversely in the tooth and can have depending on the situation various shapes. Therefore, there are different, pre-made sterilely packed membrane pads 1 to 6 which have different shapes in order to be applicable in very different situations.

The application of such a membrane pad 1 in cavity 35 of a tooth 36 is shown in more details in figure 10. When the cavity 35 was formed the pulp 38 was cut in the area 37. Thereby a horizontal area 39 around the sectional plane 37 was formed. On said horizontal area 39 the membrane 1 was positioned with the porous membrane part 7 towards the pulp. It has to be observed that the porous membrane part 7 slightly overlaps the contact surface 37 between cavity 35 and pulp 38. The membrane part 7 is then pressed to the area 39 by the carrier foil 13. The bottom side i.e. the side which is in contact with the tooth area 39, of said carrier foil is adhesive or has a structure allowing gluing so that a secure fixation of the applied membrane pad can be provided for.

The sectional drawing of figure 11 shows tooth 36 depicted in figure 10 with an applied membrane pad 1 and above the membrane pad an applied filling 40 in cavity 35. In said figure, the contact of the membrane part 7 with the edge between cavity 35 and pulp 38 can be recognized. The carrier foil 13 lies above the membrane part 7. Said carrier foil is constructed in a way that it can be pressed to the bottom side of the cavity 35 and that it provides for a seal between filling 40 and pulp 38. It is important that the margins of the defect area are sealed by a proper adaptation of the membrane margins in order to prevent lateral penetration of any undesired substances e.g. during the application of hardening sealing material which adheres to the dentine such as e.g.

light-curing glassionomer cement or during restoration of the defect of the dental hard tissues 40, respectively.

The sectional drawing of figure 12 shows tooth 36 depicted in figure 10 with an applied membrane pad which has a bilayer structure and does not comprise a carrier foil. The seal inside the cavity 35 is primarily provided for by the membrane in the dentine area surrounding the pulp. The membrane is in situ overlaid with a light-curing glassionomer cement 39 which is self adhesive to the dentine of cavity 35. The dentine defect is tightly and adhesively complemented with restoration 40.

Figure 13 shows a device 40 for the application of a medical membrane 1 in a dentine cavity 41 of a tooth 42 which cuts pulp 43. The device 40 comprises a handle 44 to which a skeleton form 45 is removably fixed. The skeleton form 45 has preferably a shape which corresponds to the shape of a cavity e.g. hemispherical or plane in order to allow pressing of the medical membrane so that there is no marginal gap and an overlaying with e.g. a light-curing glassionomer cement is possible. In a preferred embodiment the skeleton form 45 is made of a material e.g. composite, ceramic or a polymer which after hardening remains in the cavity and becomes part of the filling. The skeleton form 45 is fixed in such a way to the handle 44 of the device so that it can easily be attached or removed by the operator.

The desired diameter of the pulp pads 1 to 6 is between 1 mm and 10 mm depending on the size of the cross section of the pulp or cavity, respectively. For a sufficient circular sealing an about 1 to 2 mm wide zone around the open pulp is necessary. Thereby, any contact at the marginal zone of the open pulp with foreign and toxic substances should be a priori prevented.

After a certain time, the applied membranes are „immured" between the overlaying material or the filling, respectively, and the tertiary dentine freshly formed on the side which is in contact with the pulp or

said membranes are in the course of time reabsorbed. The tightly enclosed membrane pad can remain in situ indefinitely and forms part of the filling.

The bottom side of the pulp pad corresponds to the structure of known medical membranes wherein an average diameter of the pores between 1 µm and 100 µm and a percentage of pores of more than 50 % are preferred. Said diameter of the pores offers to the regenerative cells and to the extracellular substances such as e.g. fibrin an impermeable support during the whole healing process. Along the fibrin fibers regenerative cells reach the surface of the membrane.

The successful treatment depends on sterile surgical work i.e. that the work is performed without a bacteria burden for the pulp and that the pulp is only in contact with the sterile membrane and that it has no contact with filling material or that it is not exposed to microorganisms penetrating from outside. Furthermore, it is important that the porous membrane part fits tightly to the dentine. Depending on the shape of the cavity the membrane can be applied to the pulp either as a convex or a concave membrane, respectively. Preferred is a membrane according to the present invention which is packed sterilely in order to allow sterile work.

The described membrane pads are of crucial importance for the medical treatment of teeth since hitherto no primary wound healing of pulp exposures could be achieved. Nowadays, the pulp is overlaid with $Ca(OH)_2$ which causes in the pulp tissue lying below a harmful necrosis and protected by said necrosis tertiary dentine is formed in the context of a inflammation reaction. This is only possible in young patients whose pulp has a good ability to regenerate. Since the pulp does not have a collateral circulation and since it is only capable of a limited defense response, the limited defense response of the pulp can not cope with bigger wound areas. In older

patients the number of dentine forming stem cells is very small and therefore the treatment was often unsuccessful.

The membrane pads according to the present invention create inside a tooth ideal preconditions for a primary wound healing of the exposed pulp. The sterile, impermeable seal, the absence of a wound treatment harming the pulp, the wound healing stimulating structure, the mechanical stability and the possibility to tightly close the edges of the wound and to complement the dentine defect immediately make it possible that even pulp exposures with a big wound area or more than one wound area can be treated successfully.

While there are shown and described presently preferred embodiments of the invention, it is to be distinctly understood that the invention is not limited thereto but may be otherwise variously embodied and practiced within the scope of the following claims.

Claims

Annex to the international preliminary examination report

1. Medical membrane (1-6) for arranging in a dentine cavity of a tooth for capping of a pulp exoposure wherein said medical membrane comprises at least one roughened surface which has a porous and/or reticular structure.

2. Medical membrane (1-6) of claim 1, wherein said membrane is essentially impermeable to a sealant or to a cement.

3. Medical membrane (1-6) of claim 1, wherein the percentage of the pores or of the mesh of the porous and/or reticular surface is higher than 20 %.

4. Medical membrane (1-6) of claim 1, wherein the average diameter of the pores and/or the width of mesh is between 0.5 µm and 200 µm.

5. Medical membrane (1-6) of claim 4, wherein said average diameter of the pores and/or the width of mesh is between 1 µm and 100 µm.

6. Medical membrane (1-6) of claim 1, wherein said membrane is self adhesive to the dentine or is adhesive to the dentine due to an adhesive coating.

7. Medical membrane (1-6) of claim 1, wherein said membrane has a surface of less than 100 mm^2.

8. Medical membrane (1-6) of claim 7, wherein said membrane has a surface of less than 50 mm^2.

9. Medical membrane (1-6) of claim 1, wherein said membrane has a thickness of less than 3 mm.

10. Medical membrane (1-6) of claim 9, wherein said membrane has a thickness of less than 0.5 mm.

11. Medical membrane of claim 1, wherein said membrane (1-6) has a round or oval shape.

12. Medical membrane of claim 1, wherein said membrane (1-6) is bent convex or concave.

13. Medical membrane (1-6) of claim 1, wherein said membrane (1-6) comprises reinforcements which make said membrane plastically deformable.

14. Medical membrane (1-6) of claim 1, wherein said membrane comprises a carrier foil which partially or fully covers and/or overlaps one side of said membrane.

15. Medical membrane (1-6) of claim 1, wherein said membrane (1-6) comprises an overlapping carrier foil (13-18) wherein said overlapping part of said carrier foil adheres to the dentine.

16. Medical membrane (1-6) of claim 1, wherein said membrane (1-6) comprises a carrier foil (13-18) which does not form any adhesive connection to a restorative material.

17. Medical membrane of claim 1, wherein said membrane (1-6) comprises a carrier foil (13-18) which does form an adhesive connection to a restorative material.

18. Medical membrane (1-6) of claim 1, wherein said membrane is made of a non-reabsorbable material, preferably polytetrafluoroethylene or titanium.

19. Medical membrane (1-6) of claim 1, wherein said membrane is made of a reabsorbable material.

20. Medical membrane (1-6) according to claim 19, wherein said membrane is made of collagen.

21. Medical membrane (1-6) of claim 1, wherein said membrane comprises an active compound or a growth factor, respectively, which have an bacteriostatic or bactericidal effect or which stimulate cell attachment, cell integration and tissue formation, respectively.

22. Medical membrane (1-6) of claim 1, wherein said membrane is impermeable to ions and to molecules.

23. A set of medical membranes (1-6) of claim 1, wherein said set comprises membranes of different size and wherein the size of said membranes is smaller than 50 mm^2.

24. A method for the application of a medical membrane in dentistry, comprising the following steps:

a) positioning of a membrane on the area of a cavity where the pulp is exposed,

b) filling the cavity above said membrane with a restorative material.

25. Method of claim 24, wherein said membrane is in contact with the dentine surrounding the area of the exposed pulp.

26. A device for the application of a medical membrane (1-6) in a cavity of a tooth comprising a handle and a removable skeleton form.

27. The device of claim 26, wherein said removable skeleton form is suitable to remain in the cavity and usable to be embedded in a filling in the cavity.

28. Kit for the treatment of pulp exposures comprising at least a medical membrane (1-6) of claims 1-22 and a device for the application of a medical membrane in a cavity of claims 26 and 27.

29. Medical membrane (1-6) for arranging in a dental cavity of a tooth for capping of a pulp exposure wherein said medical membrane comprises at least one roughened surface which is suitable for the attachment of fibrin fibers and/or for the attachment of pulp cells.

1/4

Fig. 1a

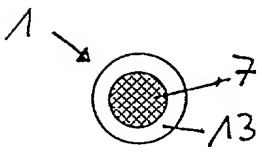


Fig. 2a

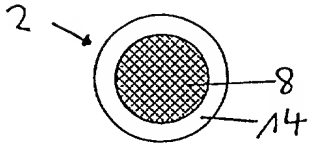


Fig. 3a

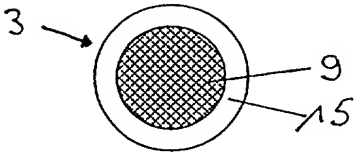


Fig.1b

Fig. 2b

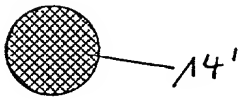


Fig. 3b

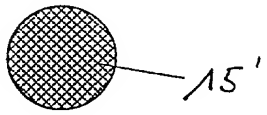
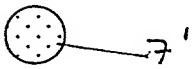


Fig. 1c



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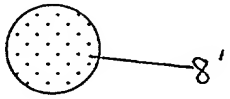


Fig. 3c

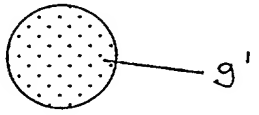
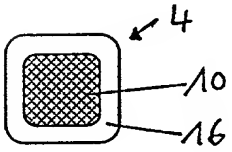


Fig. 4a



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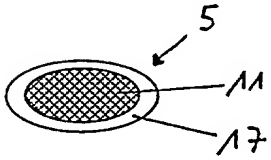

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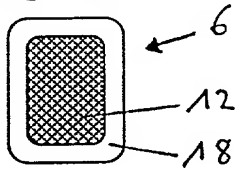


Fig. 4b

Fig. 5b

Fig. 6b

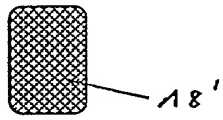


Fig. 4c

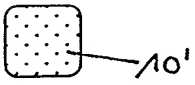


Fig. 5c

Fig. 6c

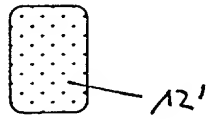


Fig-7

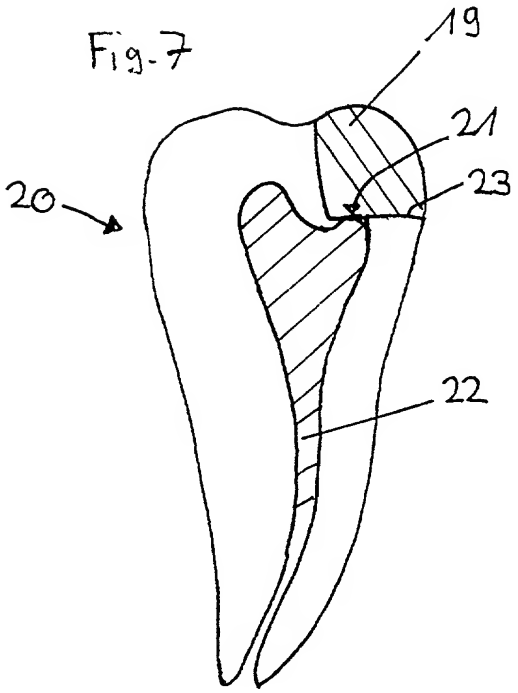


Fig. 8

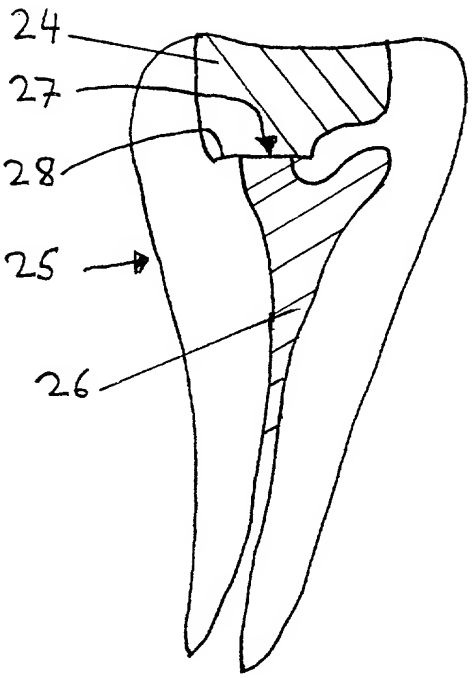


Fig. 9

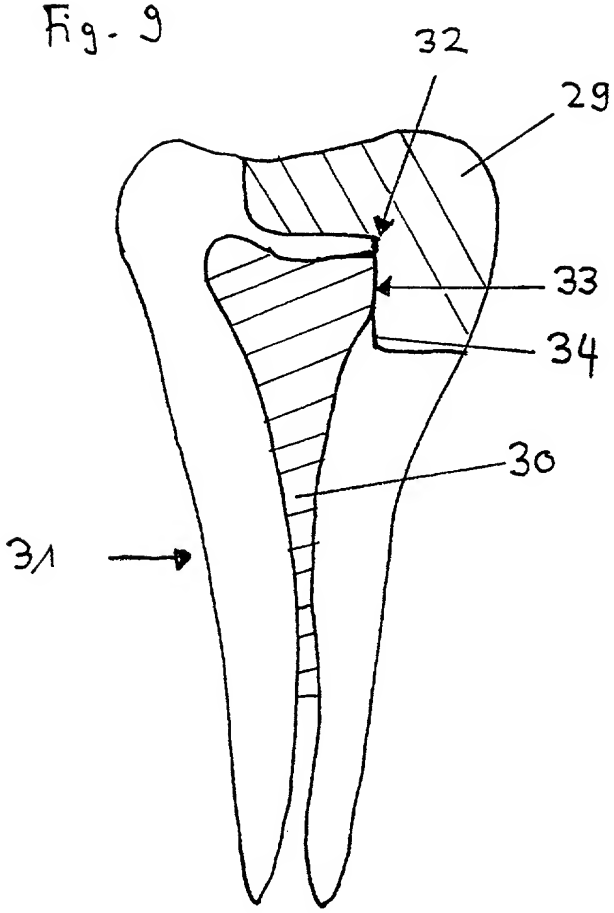


Fig. 10

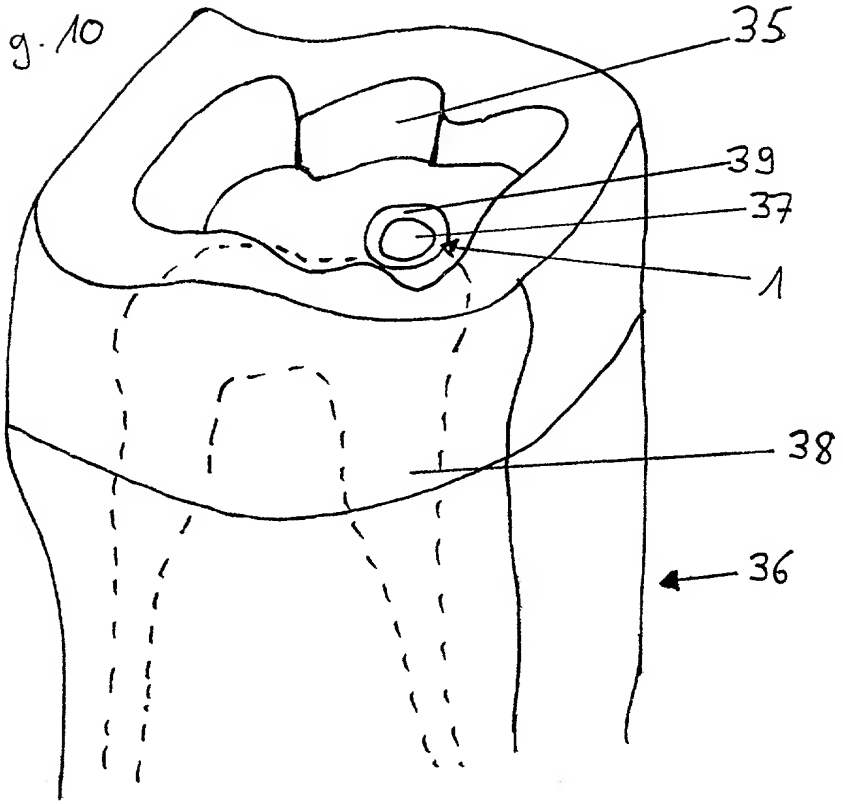


Fig. 11

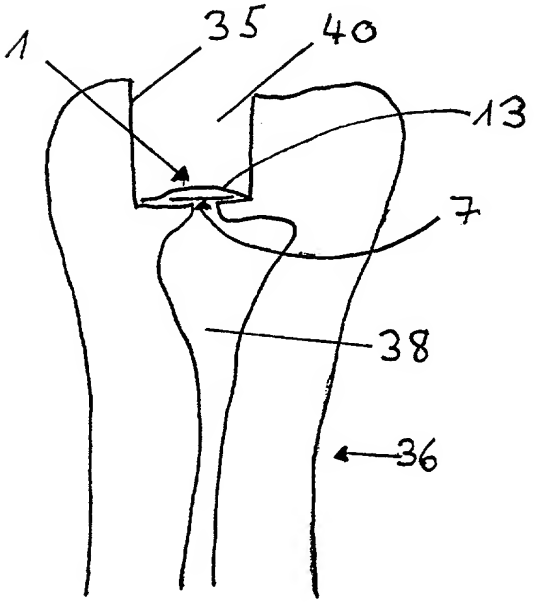


Fig. 12

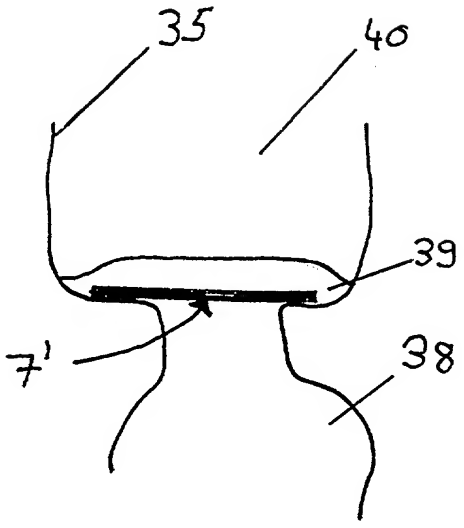
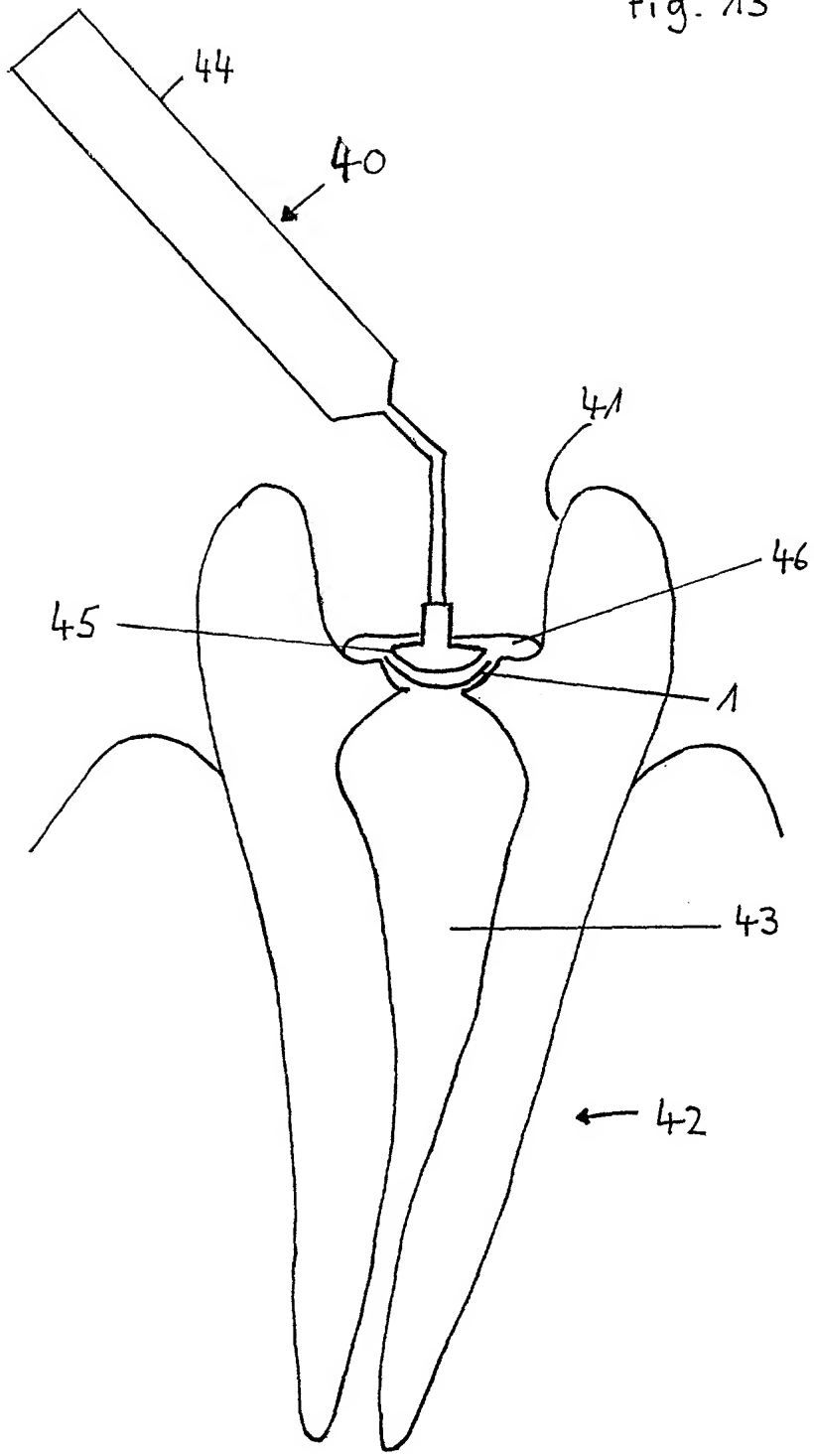


Fig. 13



Attorney Docket No. 10642.9USWO

MERCHANT & GOULD P.C.

United States Patent Application

COMBINED DECLARATION AND POWER OF ATTORNEY

As a below named inventor I hereby declare that: my residence, post office address and citizenship are as stated below next to my name; that

I verily believe I am the original, first and sole inventor (if only one name is listed below) or a joint inventor (if plural inventors are named below) of the subject matter which is claimed and for which a patent is sought on the invention entitled: MEDICAL MEMBRANE FOR STIMULATING TISSUE FORMATION

The specification of which
a. ☐ is attached hereto
b. ☒ was filed on 10 December 2001, as application serial no. and was amended on (if applicable) (in the case of a PCT-filed application) described and claimed in international no. PCT/IB00/00730 filed 31 May 2000 and as amended on 14 September 2001 (if any), which I have reviewed and for which I solicit a United States patent.

I hereby state that I have reviewed and understand the contents of the above-identified specification, including the claims, as amended by any amendment referred to above.

I hereby claim foreign priority benefits under Title 35, United States Code, § 119/365 of any foreign application(s) for patent or inventor's certificate listed below and have also identified below any foreign application for patent or inventor's certificate having a filing date before that of the application on the basis of which priority is claimed:

a. ☐ no such applications have been filed.
b. ☒ such applications have been filed as follows:

FOREIGN APPLICATION(S), IF ANY, CLAIMING PRIORITY UNDER 35 USC § 119

COUNTRY	APPLICATION NUMBER	DATE OF FILING (day, month, year)	DATE OF ISSUE (day, month, year)
Germany	199 26 438.4	10 June 1999	
Germany	199 48 787.1	10 October 1999	

ALL FOREIGN APPLICATION(S), IF ANY, FILED BEFORE THE PRIORITY APPLICATION(S)

COUNTRY	APPLICATION NUMBER	DATE OF FILING (day, month, year)	DATE OF ISSUE (day, month, year)

I hereby claim the benefit under Title 35, United States Code, § 120/365 of any United States and PCT international application(s) listed below and, insofar as the subject matter of each of the claims of this application is not disclosed in the prior United States application in the manner provided by the first paragraph of Title 35, United States Code, § 112, I acknowledge the duty to disclose material information as defined in Title 37, Code of Federal Regulations, § 1.56(a) which occurred between the filing date of the prior application and the national or PCT international filing date of this application.

U.S. APPLICATION NUMBER	DATE OF FILING (day, month, year)	STATUS (patented, pending, abandoned)

I hereby claim the benefit under Title 35, United States Code § 119(e) of any United States provisional application(s) listed below:

U.S. PROVISIONAL APPLICATION NUMBER	DATE OF FILING (Day, Month, Year)

I acknowledge the duty to disclose information that is material to the patentability of this application in accordance with Title 37, Code of Federal Regulations, § 1.56 (reprinted below):

§ 1.56 Duty to disclose information material to patentability.

(a) A patent by its very nature is affected with a public interest. The public interest is best served, and the most effective patent examination occurs when, at the time an application is being examined, the Office is aware of and evaluates the teachings of all information material to patentability. Each individual associated with the filing and prosecution of a patent application has a duty of candor and good faith in dealing with the Office, which includes a duty to disclose to the Office all information known to that individual to be material to patentability as defined in this section. The duty to disclose information exists with respect to each pending claim until the claim is canceled or withdrawn from consideration, or the application becomes abandoned. Information material to the patentability of a claim that is canceled or withdrawn from consideration need not be submitted if the information is not material to the patentability of any claim remaining under consideration in the application. There is no duty to submit information which is not material to the patentability of any existing claim. The duty to disclose all information known to be material to patentability is deemed to be satisfied if all information known to be material to patentability of any claim issued in a patent was cited by the Office or submitted to the Office in the manner prescribed by §§ 1.97(b)-(d) and 1.98. However, no patent will be granted on an application in connection with which fraud on the Office was practiced or attempted or the duty of disclosure was violated through bad faith or intentional misconduct. The Office encourages applicants to carefully examine:

(1) prior art cited in search reports of a foreign patent office in a counterpart application, and

(2) the closest information over which individuals associated with the filing or prosecution of a patent application believe any pending claim patentably defines, to make sure that any material information contained therein is disclosed to the Office.

(b) Under this section, information is material to patentability when it is not cumulative to information already of record or being made of record in the application, and

(1) It establishes, by itself or in combination with other information, a prima facie case of unpatentability of a claim; or

(2) It refutes, or is inconsistent with, a position the applicant takes in:

(i) Opposing an argument of unpatentability relied on by the Office, or

(ii) Asserting an argument of patentability.

A prima facie case of unpatentability is established when the information compels a conclusion that a claim is unpatentable under the preponderance of evidence, burden-of-proof standard, giving each term in the claim its broadest reasonable construction consistent with the specification, and before any consideration is given to evidence which may be submitted in an attempt to establish a contrary conclusion of patentability.

(c) Individuals associated with the filing or prosecution of a patent application within the meaning of this section are:

(1) Each inventor named in the application:

(2) Each attorney or agent who prepares or prosecutes the application; and

(3) Every other person who is substantively involved in the preparation or prosecution of the application and who is associated with the inventor, with the assignee or with anyone to whom there is an obligation to assign the application.

(d) Individuals other than the attorney, agent or inventor may comply with this section by disclosing information to the attorney, agent, or inventor.

(e) In any continuation-in-part application, the duty under this section includes the duty to disclose to the Office all information known to the person to be material to patentability, as defined in paragraph (b) of this section, which became available between the filing date of the prior application and the national or PCT international filing date of the continuation-in-part application.

I hereby appoint the following attorney(s) and/or patent agent(s) to prosecute this application and to transact all business in the Patent and Trademark Office connected herewith:

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[illegible]ignault, Ronald A.	Reg. No. 25,968	Pytel, Melissa J.	Reg. No. 41,512
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[illegible]Pietro, Mark J.	Reg. No. 28,707	Samuels, Lisa A.	Reg. No. 43,080
Doscotch, Matthew A.	Reg No. P-48,957	Schmaltz, David G.	Reg. No. 39,828
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[illegible]ilson, Randall A.	Reg. No. 31,838	Underhill, Albert L.	Reg. No. 27,403
Holzer, Jr., Richard J.	Reg. No. 42,668	Vandenburgh, J. Derek	Reg. No. 32,179
Hope, Leonard J.	Reg. No. 44,774	Wahl, John R.	Reg. No. 33,044
Jardine, John S.	Reg. No. P-48,835	Weaver, Paul L.	Reg. No. 48,640
[illegible]hns, Nicholas P.	Reg. No. 48,995	Welter, Paul A.	Reg. No. 20,890
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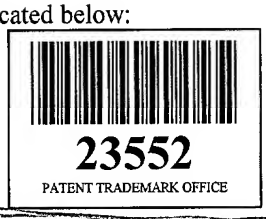
Keys, Jeramie J.	Reg. No. 42,724	Withers, James D.	Reg. No. 40,376
Knearl, Homer L.	Reg. No. 21,197	Witt, Jonelle	Reg. No. 41,980
Kowalchyk, Alan W.	Reg. No. 31,535	Wong, Thomas S.	Reg. No. 48,577
Kowalchyk, Katherine M.	Reg. No. 36,848	Wu, Tong	Reg. No. 43,361
Lacy, Paul E.	Reg. No. 38,946	Young, Thomas	Reg. No. 25,796
Larson, James A.	Reg. No. 40,443	Zeuli, Anthony R.	Reg. No. 45,255

I hereby authorize them to act and rely on instructions from and communicate directly with the person/assignee/attorney/firm/ organization who/which first sends/sent this case to them and by whom/which I hereby declare that I have consented after full disclosure to be represented unless/until I instruct Merchant & Gould P.C. to the contrary. I understand that the execution of this document, and the grant of a power of attorney, does not in itself establish an attorney-client relationship between the undersigned and the law firm Merchant & Gould P.C., or any of its attorneys.

Please direct all correspondence in this case to Merchant & Gould P.C. at the address indicated below:

Merchant & Gould P.C.
P.O. Box 2903
Minneapolis, MN 55402-0903



I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

2	**Full Name Of Inventor**	**Family Name** HORVATH	**First Given Name** Domonkos	**Second Given Name**
0	**Residence & Citizenship**	**City** Jestetten	**State or Foreign Country** Germany DEX	**Country of Citizenship** Germany
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Signature of Inventor 201:				**Date:** 27.12.2001

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